Theories on GDF11's MOA in suppressing HSA and why higher doses may be necessary with active bleeds and tumors

We have seen recently that mega dosing of HSA dogs with GDF11 during a bleed is effective in stopping the bleed and eventually eliminating the HSA tumor(s). There are so many questions to be answered – why and how does GDF11 work on HSA tumors and do big doses really help or are they detrimental?

Anecdotally, we have seen dogs with active bleeds who seem to be able to tolerate much larger doses of GDF11. As you know, the first sign of excess GDF11 is insomnia, so let's take a look at that.

As far as what researchers have to say on the subject, let's take a look at a couple of GDF11 papers that are relevant to defeating HSA. You will be happy to know that they both support our work, more or less.

Check out GDF11 Implications in Cancer Biology and Metabolism. Facts and Controversies

In the abstract section, note it says "*A blunt fact regarding GDF11 biology is that its target cells have stemness features, a property that could be found in certain adult cells in health and in disease, such as cancer cells*."

In the Intro it says "*If GDF11 targets cells with stemness capacity, then many cancer cells should be targeted by this growth factor*".

If the above two statements are true, then we are certainly on the right track. Also, the 2nd quote does indirectly imply why much bigger doses of GDF11 are necessary to defeat HSA tumors. There are surely hundreds of billions of cancer cells in even a small HSA tumor, so if GDF11 is targeting these cancer cells, you are going to need a lot more of it than a healthy dog/person would require.

The paper goes on to say that GDF11 induces tumor suppressive properties in liver, breast cancer and pancreatic cancer which is good news for us. Though it appears that higher GDF11 levels result in a worse outcome for those with colorectal cancer.

In the metabolism section there is more good news "*In fact, it is reported that GDF11 impairs mitochondrial function in cancer cell lines, particularly in HCC-derived cells (14). The impact of GDF11 in the central metabolic organelle could explain the tumor suppressive properties exerted by the growth factor*".

Impairment of mitochondrial function should halt most tumor cell replication and can easily result in HSA tumor cell death.

Now check out GDF11 exhibits tumor suppressive properties in hepatocellular carcinoma cells by restricting clonal expansion and invasion

This paper posits that GDF11 would be a good treatment for human liver cancer.

Highlights of the paper include:

• GDF11 restricts cancer cell proliferation in liver cancer cells.

• GDF11 induces cell cycle arrest decreasing Cyclin D1, A and cdk6 and increasing 27.

• GDF11 induces mesenchymal to epithelial transition.

• GDF11 diminishes cell invasion.

The third bullet point is supported by this statement "*The immunoblot revealed a decrement of mesenchymal markers, such as Snail and N-cadherin, and the increment of epithelial markers, such as occludin and E-cadherin, in a time-dependent manner"*

Since HSA is largely a cancer of the epithelium (lining of blood vessels) , anything that results in epithelial repair is good news for us.

In summary, the two papers mentioned above do support our exogenous GDF11 administration to HSA dogs. However, they don't address the tough part which is the GDF11 dosing protocol. That's for us GDF11 HSA pioneers to figure out. Tough challenge, but we've made decent progress so far and I know we will continue to do so.